

-continued

primer

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We claim:

1. A screening method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:
 - (i) expressing a peptide, polypeptide or protein in the plasma membrane of a host cell, said peptide, polypeptide or protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell;
 - (ii) contacting said host cell with the test substance; and
 - (iii) determining changes to the ion channel activity of said heterologous protein induced by the test substance, wherein the changes to the ion channel activity of the heterologous protein induced by the test substance are determined by detecting the effect of the test substance on changes in net movement across the plasma membrane of the host cell of small cellular metabolite molecules which do not directly permeate the ion channel formed by said heterologous protein.
2. A method according to claim 1, wherein the effect of the test substance on changes in the net movement of proline or adenine molecules across the plasma membrane is detected.
3. A method according to claim 1, wherein said host cell is *E. coli*.
4. A method according to claim 1, wherein said substance having ion channel activity is a heterologous cation channel protein.
5. A method according to claim 4, wherein said substance having ion channel activity is a heterologous sodium channel protein.
6. A method according to claim 4, wherein said substance having ion channel activity is the HIV-1 Vpu integral membrane protein.
7. A method according to claim 1, wherein leakage of said small cellular metabolite molecules from the host cell is detected.
8. A method according to claim 7, wherein leakage of said small cellular metabolite molecules from the host cells is detected by either:
 - (i) cross-feeding of cells which are auxotrophic for the leaked metabolite; or
 - (ii) failure of cells expressing the ion channel to grow in the absence of the leaking metabolite being supplied in the external medium.
9. A method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:
 - (i) expressing HIV-1 Vpu integral membrane protein in the plasma membrane of a host cell, said protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell;
 - (ii) contacting said host cell with the test substance; and
 - (iii) determining changes to the ion channel activity of said heterologous protein induced by the test substance, wherein the changes to the ion channel activity of the heterologous protein induced by the test substance are determined by detecting the effect of the test substance on changes in net movement across the plasma membrane of the host cell of small cellular metabolite molecules.
10. The method of claim 9 wherein the effect of the test substance on changes in the permeability of the plasma membrane to proline or adenine molecules is detected.
11. The method of claim 9 wherein said host cell is *E. coli*.
12. The method of claim 9 wherein leakage of metabolite from the host cell is detected.
13. The method of claim 12 wherein leakage of metabolite from the host cells is detected by either:
 - (i) cross-feeding of cells which are auxotrophic for the leaked metabolite; or
 - (ii) failure of cells expressing the ion channel to grow in the absence of the leaking metabolite being supplied in the external medium.
14. A screening method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:
 - (i) expressing HIV-1 Vpu integral membrane protein in the plasma membrane of a host cell, said protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell;
 - (ii) contacting said host cell with the test substance; and
 - (iii) determining changes to the ion channel activity of said heterologous protein induced by the test substance, wherein the changes to the ion channel activity of the heterologous protein induced by the test substance are determined by detecting the effect of the test substance on changes in net movement across the plasma membrane of the host cell of small cellular metabolite molecules.
15. The method of claim 14 wherein the effect of the test substance on changes in the movement of proline or adenine molecules is detected.

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16. The method of claim 14 wherein said host cell is *E. coli*.

17. The method of claim 14 wherein leakage of metabolite from the host cell is detected.

18. The method of claim 17 wherein leakage of metabolite from the host cells is detected by either:

(i) cross-feeding of cells which are auxotrophic for the leaked metabolite; or

(ii) failure of cells expressing the ion channel to grow in the absence of the leaking metabolite being supplied in the external medium.

19. A screening method for determining ion channel modulating activity of a test substance having potential for such modulating activity, which comprises the steps of:

(i) expressing HIV-1 Vpu integral membrane protein in the plasma membrane of a host cell, said protein having ion channel activity when expressed as a heterologous protein in the plasma membrane of the host cell;

(ii) contacting said host cell with the test substance; and

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(iii) determining changes to the ion channel activity of said heterologous protein induced by the test substance.

20. The method of claim 19 wherein the effect of the test substance on changes in the permeability of the plasma membrane to proline or adenine molecules is detected.

21. The method of claim 19 wherein said host cell is *E. coli*.

22. The method of claim 19 wherein leakage of metabolite from the host cell is detected.

23. The method of claim 22 wherein leakage of metabolite from the host cells is detected by either:

(i) cross-feeding of cells which are auxotrophic for the leaked metabolite; or

(ii) failure of cells expressing the ion channel to grow in the absence of the leaking metabolite being supplied in the external medium.

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